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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,909	10/29/2003	James B. Lorens	021044-005820US	9257
20350	7590	08/14/2007	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP			REDDIG, PETER J	
TWO EMBARCADERO CENTER			ART UNIT	PAPER NUMBER
EIGHTH FLOOR			1642	
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			08/14/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action Before the Filing of an Appeal Brief</b>	Application No.	Applicant(s)
	10/696,909	LORENS ET AL.
	Examiner Peter J. Reddig	Art Unit 1642

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

THE REPLY FILED 09 July 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a)  The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.

b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2.  The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because

(a)  They raise new issues that would require further consideration and/or search (see NOTE below);

(b)  They raise the issue of new matter (see NOTE below);

(c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.

6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: \_\_\_\_\_.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

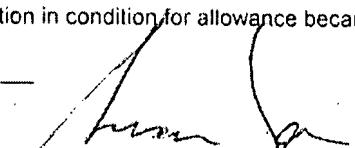
10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because:

12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.

13.  Other: \_\_\_\_\_.

  
SUSAN L. H. D.  
PRIMARY EXAMINER

Continuation of 3. NOTE: The amendments to claim 1 of "determining, in the presence and absence of the compound, in vitro kinase activity", and step 2 wherein an "angiogenesis phenotype assay" is performed in combination with the in vitro kinase activity assay would require an additional search. Additionally, step 2 wherein an "angiogenesis phenotype assay" is performed in combination with the in vitro kinase activity assay raises the issue of new matter/ written description. Furthermore, amended claim 12, now drawn to tube formation would require further search and consideration. Furthermore, amended claim 27 and 55 would require additional search for "down regulation of Axl polypeptide inhibits a cell-based angiogenesis phenotype assay" or "inhibition of the angiogenesis phenotype in the cell based angiogenesis assay is caused by down regulation of expression of the angiogenesis polypeptide", wherein the angiogenesis phenotype assays appear to include endothelial cell tube formation assays, as well as other bioassays such as the chick CAM assay, the mouse corneal assay, haptotaxis assays, VEGF-R assays, co-culture tube formation assays, see para 0085 of the published application.

If the amendment were entered, claims 1, 12, and 14-18 would remain rejected under 35 USC 112 for the reasons previously set forth in the Office Action of 8/23/06, pages 4-10, and the Office action of 5/7/07, pages 2-6.

Applicants argue that support for the protein with 95% identity to full length SEQ ID NO: 4 is provided by SEQ ID NO: 4, the fact the Axl is well known and sequence algorithms and kinase assays can be used to identify polypeptides that fall within the scope of the claims. Applicants argue that down regulation of Axl polypeptide results in an inhibition of a number of cell-based angiogenesis assays.

Applicants arguments have been considered, but have not been found persuasive because Applicants are reiterating arguments previously set forth and found to be non-persuasive for the reasons of record and arguments directed to the in vitro kinase activity and cell-based angiogenesis assays are moot due to the non-entry of the amendment, thus the claims remain rejected for the reasons previously set forth.

Applicants argue that both Sun and Bandman require an Examiner to base a rejection for alleged lack of enablement on a specific explanation or evidence of why the claimed molecule would not maintain an asserted activity after mutation of, e.g., 5% of the amino acid sequence. Sun at page 7 and Bandman at page 15. Applicants have SEQ ID NO: 4, and, to identify proteins with 95% identity to SEQ ID NO: 4, well-known sequence analysis algorithms are disclosed at page 11, lines 15-23. Axl was known to be a tyrosine kinase at the time of filing, and angiogenesis assays that are regulated by Axl are disclosed and demonstrated. Applicants argue that the Office Action has not provided sufficient analysis or evidence to demonstrate that one of skill, using the information in the specification and literature at the time of filing, would not be able to make and use the genus of Axl polypeptides with 95% identity to SEQ ID NO: 4.

Applicants arguments have been considered, but have not been found persuasive because Applicants are reiterating arguments previously set forth and found to be non-persuasive for the reasons of record and are arguing limitations in the non-entered amendment, the asserted activities (in vitro kinase activity and cell based-angiogenesis phenotype assay). Furthermore, the citations of Sun at page 7 and Bandman at page 15 do not appear to be relevant to the instant rejection in that Sun at page 7 is simply a summary of the arguments and Bandman at page 15 is just an address.

If the amendment were entered, claims 1, 12, and 14-18 would remain rejected under 35 USC 112 for the reasons previously set forth in the Office Action of 5/7/07, pages 15-19.

Applicants argue that claim 1 has been amended to include the step of inhibition of a cell-based angiogenesis phenotype assay in the presence of the compound.

Applicants' arguments have been considered, but have not been found persuasive because are arguing limitations in the non-entered amendment.

If the amendment were entered, claims 1, 12, and 14-18 would remain rejected for lacking an adequate written description under 35 USC 112 for the reasons previously set forth in the Office Action of 8/23/06, pages 21-24 and in the Office Action of 5/7/07, pages 7-10.

Applicants argue that the specification does provide descriptive support for the full scope of the claimed invention by providing both SEQ ID NO: 4, a reference sequence for the recited polypeptides, and assays for regulation and inhibition of angiogenesis. Axl kinase activity was well known at the time of filing. Applicants argue that the assays are described throughout the specification.

Applicants arguments have been considered, but have not been found persuasive because Applicants are reiterating arguments previously set forth and found to be non-persuasive for the reasons of record and are arguing limitations in the non-entered amendment, i.e. the asserted activities (in vitro kinase activity and cell based-angiogenesis phenotype assay), thus the claims remain rejected for the reasons previously set forth.

Applicants argue that both Sun and Bandman require an Examiner to base a rejection for alleged lack of written description on a specific explanation or evidence of why the claimed molecule would not maintain an asserted activity after mutation of, e.g., 5% of the amino acid sequence. Sun at page 9 and Bandman at page 5. In particular, the Board in Sun indicated that identification of conserved areas of a protein and functions of those areas sufficiently supports a claim to a genus of polypeptides with 80% identity to the reference sequence. Sun at page 10. Similar information is provided in Figure 11, which discloses Ig binding regions FN3 regions and the tyrosine kinase domain of the Axl protein. According to Sun, this type information is sufficient to provide descriptive support of the claimed genus.

Applicants' arguments have been considered, but have not been found persuasive because Applicants are arguing limitations in the non-entered amendment, i.e. the asserted activities (in vitro kinase activity and cell based-angiogenesis phenotype assay). Furthermore, the specification does not teach the areas of SEQ ID NO: 4 that can be disturbed without affecting its function and the claims are not drawn naturally occurring amino acid sequences as previously set forth.

Applicants argue that the Office Action also disputes that Example 14 of the Synopsis of Application of Written Description Guidelines applies to the claims. In response, Applicants assert that the amended claims recite kinase activity of the Axl protein and an assay for inhibition of an angiogenesis phenotype caused by the inhibition of the Axl protein. The Synopsis indicates that a "single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay...." that could be used to identify members of the claimed genus. The amended claims thus follow the guidelines for written description put forth by the US Patent Office.

Applicants' arguments have been considered, but have not been found persuasive because Applicants are reiterating arguments previously set forth and found to be non-persuasive for the reasons of record and are arguing limitations in the non-entered amendment, i.e. the asserted activities (in vitro kinase activity and cell based angiogenesis phenotype assay), thus the claims remain rejected for the reasons previously set forth.

If the amendment were entered, claims 1,14 and 54 would remain rejected under 35 USC 102 for the reasons previously set forth in the Office action of 5/7/07, pages 10-12.

Applicants argue that Healy et al. do not teach every element of the amended claims, even in view of Gallicio et al.

Applicants' arguments have been considered, but have not been found persuasive because Applicants are arguing limitations in the non-entered amendment.

If the amendment were entered, claims 12 and 15-18 would remain rejected under 35 USC 103(a) for the reasons previously set forth in the Office Action of 8/23/06, pages 4-10, and the Office action of 5/7/07, pages 12-14.

Applicants argue that Healy et al, Varner and Cheresh, Panzer et al. and Ruoslahti et al. do not teach every element of the amended claims, and do not provide motivation to combine the individual references. Applicants argue that none of the reference discloses that Axl has any role in angiogenesis.

Applicants' arguments have been considered, but have not been found persuasive because Applicants are arguing limitations in the non-entered amendment and are reiterating arguments previously set forth and found to be non-persuasive for the reasons of record, thus the claims remain rejected for the reasons previously set forth. Additionally, Applicants appear to suggest that the studies of Healy et al. of Gas-6 and Axl and endothelial cell survival does not have anything to do with angiogenesis which is clearly not the case in view of the prior art which routinely uses cultured endothelial cells to study angiogenesis.